960-66 Enalapril (EN) Improves Alveolar-Capillary Diffusion in Chronic Heart Failure (CHF) and Aspirin (AS) Contrasts This Effect

Marco Guazzi, Pier G. Agostoni, Gian C. Marenzi, Gian F. Lauri, Emilio Assanelli, Maurizio D. Guazzi. *University of Milan, Milan, Italy*

Prostaglandins (PGs) participate in the local control of transcapillary fluid flux and interstitial volume. ACE is concentrated in the lung vessels and ACE-inhibitors expose them to enhanced formation of PGs. Were PGs involved in the regulation of extravascular lung fluid, ACE inhibitors and AS would probably exert an opposite therapeutic action in CHF, where lung fluid plays a pivotal role. To probe this assumption 15 CHF patients (III, NYHA), treated with digoxin and furosemide, received (random and double-blind) placebo (PL), EN (20 mg), AS (325 mg), EN + AS, for 15 days each. Vital capacity (VC), maximal voluntary ventilation (MVV), lung diffusing capacity (DLCO) and oxygen consumption (VO2p), ventilation (VEp), tidal volume, (VTp), dead space/tidal volume ratio (VD/VT) at peak exercise were tested at the end of each step.

	VO2 p	VE p	VT p	VD/VT	MVV	VC	DLCO
PL	15.0	47.9	1.49	0.23	89	3.1	22
	± 5	± 15	± 0.4	± 0.6	± 24	± 7	± 7
EN	18.8	64	1.71	0.20	104	3.2	24
	± 4*#§	± 12*#§	± 0.3*#§	± 6*§	± 21*	± 6	± 6*§#
AS	15.8	50	1.50	0.24	93	3.0	22
	± 4	± 15	± 0.3	± 0.6	± 21	± 7	± 7
EN + AS	16.7	54.8	1.54	0.22	103	3.1	22
	± 4	± 12	± 0.9	± 0.5	± 24*	± 6	± 7

Means ± SD, *p < 0.05 vs PL; §p < 0.05 vs AS; #p < 0.05 vs EN + AS

Conclusions: a) Changes in DLCO and lung mechanics with EN are consistent with modulation of lung interstitial fluid, ameliorating respiratory and functional capacities; b) PG stimulation seems to underlie these actions as they are counteracted by a PG inhibitor.

960-67 C-Myc Expression Relates to Decrease in Myocardial Contractility in Patients With Chronic Aortic Regurgitation

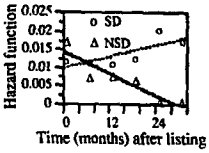
Satoshi Taketani, Kazuhiro Taniguchi, Yoshiki Sawa, Keiji Kadoba, Masataka Mitsuno, Hikaru Matsuda, Shunzo Onishi [1], Naomasa Kawaguchi [1, 1] *1st Dept of Surg, School of Allied Health Science, Osaka Univ., Osaka, Japan*

In patients with end-stage aortic regurgitation (AR), excess of volume-load on the left ventricle (LV) cause congestive heart failure associated with a decrease in LV contractility. Recently, proto-oncogenes have been implicated in the pathogenesis of myocardial remodeling resulting in a decrease in LV contractility. However, in human heart, it has never been clarified whether C-Myc may relate to contractile impairment and structural alteration. In the present study, the expression of C-Myc in myocardium were examined in patients with AR. Nine patients (7 male and 2 female) aged from 31 to 70 years (mean, 52.9 ± 13.4) with isolated chronic AR underwent aortic valve replacement. Preoperative NYHA class was III in 5 patients and IV in 4. Ejection fraction of LV (EF)(49.2 ± 11.6%), end-systolic volume index of LV (ESVI)(87 ± 30 ml/m^2) and left ventricular mass index (LVMI)(183 ± 34 g/m^2) were measured before surgery. The specimens of LV muscle were obtained by endomyocardial biopsy during aortic valve replacement. Expression of C-Myc were evaluated by immunohistochemical staining. All patients showed significant higher values in myocardial cell diameter (CD)(33.1 ± 11.8 μm)and fibrous content (FC)(26.5 ± 13.2 g/m^2) than did the normal control. C-Myc(28.3 ± 16.1%) was detected in these patients while, it has never been detected in normal control. ESVI were inversely correlated with EF($r = 0.94$ $p < 0.01$), CD ($r = 0.93$ $p < 0.01$) and FC($r = 0.95$ $p < 0.01$). C-Myc showed inverse correlation with ESVI($r = -0.87$ $p < 0.05$), CD($r = 0.96$ $p < 0.01$) and FC($r = 0.92$ $p < 0.01$). These results demonstrated that C-Myc expression relate to extensive cellular hypertrophy and interstitial fibrosis and inversely relate to ESVI in patients with chronic aortic regurgitation. This suggest that C-Myc may relate to cardiac remodeling, and its down-regulation may be associated with the decrease in LV contractility.

960-68 Differences in Temporal Risk of Sudden and Nonsudden Death in Patients With End-Stage Heart Failure Listed for Cardiac Transplantation

Michael O. Sweeney, John B. Newell, Hasan Garan, Brian McGovern, Marc J. Semigran, Jeremy N. Ruskin, G. William Dec. *Massachusetts General Hospital, Boston, MA*

Sudden death (SD) is a major threat to survival in patients with end-stage heart failure awaiting cardiac transplantation. Current prioritization of recipient need for transplantation is based on criteria relating to hemodynamic compensation and risk of nonsudden death (NSD). Similar criteria for stratifying risk of SD do not exist and the temporal pattern of SD risk is unknown. We compared actuarial SD and NSD mortality rates in 162 patients listed for transplantation using lifetable analysis. There were 43/162 (26.5%) cardiac deaths [23(14.2%) sudden and 20(12.3%) nonsudden] during mean followup 15.8 ± 18.3 months. Hazard functions derived from lifetable analysis were plotted as a function of time and the equations of the best-fit lines were calculated by linear regression (Figure).



The slope of the hazard function curve expresses the change in (probability of death/month per month) independent of censored events (transplantation). The SD slope was positive (+0.03 ± 0.01, R = 0.81, p = 0.04) and the NSD slope was negative (– 0.05 ± 0.01, Time (months) after listing R = 0.92, p = 0.01) consistent with progressively increasing versus progressively decreasing rates of change in risk, respectively.

Conclusions: In patients with end-stage heart failure listed and awaiting transplantation, the risk of NSD decreases over time, while in contrast, the risk of SD increases over time.

961 Role of Vasospasm

Tuesday, March 26, 1996, Noon–2:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: Noon–1:00 p.m.

961-69 Contribution of Coronary Vasoconstriction to Myocardial Blood Flow Changes Induced by Physiologic Stresses

Asif Rehman, Anastasia N. Kitsiou, Stephen L. Bacharach, Claiborne M. Davis, Vasken Dilsizian, Arshed A. Quyyumi. *NIH, Bethesda, MD*

Atherosclerotic coronary arteries constrict in response to exercise (EX). We investigated the impact of coronary vasoconstriction on regional myocardial blood flow (MBF) in normal and ischemic zones during physiologic stresses including bicycle EX, mental stress (MS) using a video game, and compared it with adenosine (ADO). Seven men (age 60 ± 10 years; 5 with 2- and 2 with 3-vessel CAD) had MBF estimated from N-13 ammonia uptake normalized to absolute flow in one sector using PET. All pts had normal left ventricular function (ejection fraction 56 ± 8%) and EX-induced thallium perfusion defects. Ischemic segments were defined as regions where ADO-induced MBF increase was < 90% of normal segments (supplied by unobstructed coronaries). MBF changes with EX and MS were compared with ADO in 171 normal and 101 ischemic segments. (MBF in ml/min/g)

	Rest	ADO	MS	EX
MBF (Normal zones)	0.62	2.6	1.2	1.7
MBF (Ischemic zones)	0.75*	1.9**	1.1*	1.3*

*p < 0.05, **p < 0.01

MBF was lower in ischemic segments at rest, and after MS and EX. Despite development of ischemia (ST depression) during EX which would be expected to maximize blood flow, MBF in the ischemic segments remained 29% below the level achieved with ADO (that measures flow reserve). Similarly, during MS, MBF in ischemic segments was lower than in normal areas, and much lower than ADO, suggesting that coronary vasoconstriction in ischemic regions occurs during both EX and MS. Thus, vasoconstriction of coronary stenoses during EX and MS causes significant attenuation in MBF increases to ischemic regions. Whether these changes can be reversed by antianginal medications needs to be further investigated.

961-70 Role of Basal Coronary Tone in Vasospastic Angina

Yukio Ozaki, David Keane, Patrick W. Serruys. *Catheterization Laboratory, Thoraxcenter, Erasmus University Rotterdam, NL*

Previous attempts to determine the role of basal coronary tone in the pathophysiology of variant angina have produced conflicting evidence. We examined the vasoconstrictor response to ergonovine and the vasodilator response to isosorbide dinitrate (basal coronary tone) at spastic and non-